In claim 14, line 1, delete ",5, 6, 7, 8, 9 and 10" and insert therefor –and 5--.

--20. (new) A method of inhibiting the inflammatory activity IL-1β upstream of TNF-α comprising the step of administering a pharmaceutically effective amount of a lactoferrin product.--

REMARKS

Claims 1-20 are pending in the present application. Claims 1 and 5-7 are rejected. Claims 8-10 and 12-14 are objected to. Claims 2-4, 11 and 15-19 are withdrawn from consideration. Claim 20 is newly presented for examination in the present Amendment and Response. No issue of new matter arises by way of this amendment since express support for the recitation that lactoferrin works downstream of IL-1β and upstream of TNF-α to inhibit the immune response is set forth in the present specification at page 8, lines 10-12 among other places.

Regarding the Restriction Requirement

The Examiner acknowledges the Response to the Restriction Requirement filed on December 20, 1999. The Examiner maintains that the inventions are distinct as stated in the Restriction Requirement of October 4, 1999. The Restriction Requirement is made final. Claims 2-4, 11, and 15-19 are therefore withdrawn from further consideration.

Objection to the Specification

The Examiner objects to the disclosure because at page 35, line 4 d "oxaolone/lactoferrin:" should be "Oxaolone/-lactoferrin:". Applicants herein correct this minor grammatical error thereby obviating the objection.

Objection to the Claims

The Examiner objects to claims 8-10 and 12-14 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. Applicants herein correct this minor formality matter by changing claims 8-10 and 12-14 to depend only from the independent claims, namely claims 1 and 5.

Rejection under 35 U.S.C. §103(a)

The Examiner rejects claims 1 and 5-7 under 35 U.S.C. §103(a).

Regarding claim 1

The Examiner rejects claim 1 under 35 U.S.C. 103(a) as being unpatentable over Teng *et al.* in view of Nuijens *et al.* and Enk *et al.* (Proc. Natl. Acad. Sci. USA, Vol 89, pp 1398-1402), and Penco *et al.* The Examiner says that Teng *et al.* teach a method of treating dermal inflammatory disorder comprising the step of administering a pharmaceutically effective amount of a lactoferrin product (citing page 4, lines 21-30). The Examiner admits that Teng *et al.* do not teach using this method to inhibit the inflammatory activity of IL-1β in inflammatory dermal disorders. However, the Examiner says that Nuijens *et al.* teach that lactoferrin reduces the production of IL-1β and TNFα and inhibits proliferation (citing page 287, third paragraph). The Examiner adds that Enk *et al.* teach that both IL-1β and TNFα are responsible for promoting inflammatory activity, including allergen-induced inflammatory activity (citing the abstract). Moreover, the Examiner says that Penco *et al.* teach that lactoferrin inhibits the activity of IL-1β (citing the abstract). Therefore, the Examiner maintains that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use the method of Teng *et al.* for inhibiting the dermal inflammatory activity of IL-1β. The Examiner says that a person of ordinary skill in the art would have been motivated to use the method of Teng *et al.* for inhibiting the dermal inflammatory activity of IL-1β because lactoferrin is known for reducing the production of IL-1β and TNFα and inhibiting the activity of IL-1β.

Respectfully, Applicants submit that Teng *et al.* do not teach a method of treating dermal inflammatory disorder comprising the step of administering a pharmaceutically effective amount of a lactoferrin product as the Examiner contends. Teng *et al.* generally say that lactoferrin may be used to treat a deficiency of lactoferrin in a patient at page 4, lines 21-30. This is merely a generic statement. Even this generic statement is not enabled by the reference. In order for a reference to be valid, it must be enabling for the statements made therein. Teng *et al.* is simply not enabling for treating dermal inflammatory disorder by administering a pharmaceutically effective amount of a lactoferrin product. At most, Teng *et al.* provide an invitation to try to treat lactoferrin deficiency. However, Teng *et al.* do not even provide an invitation to try to treat dermal inflammatory disorder by administering lactoferrin. Certainly, Teng *et al.* provide no reasonable expectation that such treatment would be successful.

The deficiencies of Teng *et al.* as set forth, *supra*, are not cured by any of the secondary references cited. Hence, a proper *prima facie* case of obviousness has not been set forth as required for a rejection under 35 U.S.C. §103(a). In short, it would not have been obvious to a person of ordinary skill in the art to use lactoferrin to inhibit the inflammatory

activity of IL-1β as specifically claimed in claim 1.

Regarding claims 5-7

The Examiner rejects claims 5-7 under 35 U.S.C. 103(a) as being unpatentable over Teng *et al.* in view of Nuijens *et al.* and Enk *et al.* (Proc. Natl. Acad. Sci. USA, Vol 89, pp 1398-1402). According to the Examiner, Teng *et al.* teach a method of treating dermal inflammatory disorder of humans comprising the step of administering a pharmaceutically effective amount of a lactoferrin product (citing page 4, lines 21-30). The Examiner admits that Teng, *et al.* do not teach using this method to treat an allergen-induced dermal inflammatory disorder. However, the Examiner says that Nuijens *et al.* teach that lactoferrin reduces the production of IL-1β and TNF-α and inhibits proliferation (citing page 287, third paragraph). The Examiner says that Enk *et al.* teach that both IL-1β and TNF-α are responsible for promoting inflammatory activity, including the allergen-induced inflammatory activity (citing the abstract). Therefore, the Examiner maintains that it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to use the method of Teng *et al.* for treating an allergen-induced dermal inflammatory disorder. The Examiner contends that a person of ordinary skill in the art would have been motivated to use the method of Teng *et al.* for treating an allergen-induced dermal inflammatory disorder because lactoferrin is known for reducing the production of IL-1β and TNFα and inhibiting the activity of IL-1β.

As set forth, *supra*, regarding claim 1, Teng *et al.* do not teach a method of treating dermal inflammatory disorder comprising the step of administering a pharmaceutically effective amount of a lactoferrin product as the Examiner contends. Teng *et al.* generally say that lactoferrin may be used to treat a deficiency of lactoferrin in a patient at page 4, lines 21-30. This is merely a generic statement. Even this generic statement is not enabled by the reference. In order for a reference to be valid, it must be enabling for the statements made therein. Teng *et al.* is simply not enabling for treating dermal inflammatory disorder by administering a pharmaceutically effective amount of a lactoferrin product. At most, Teng *et al.* provide an invitation to try to treat lactoferrin deficiency. However, Teng *et al.* do not even provide an invitation to try to treat dermal inflammatory disorder or an allergen-induced inflammatory disorder by administering lactoferrin. Certainly, Teng *et al.* provide no reasonable expectation that such treatment would be successful.

Applicants respectfully submit that none of the cited references teach that lactoferrin suppresses the induction of allergen dependent inflammatory responses as set forth in the present specification at page 3, lines 15-16 among other places and as specifically recited in claim 5 and claims 6 and 7 by virtue of dependency from claim 5. (Applicants herein amend claim 7 to depend from claim 5 only in order to insure proper antecedent basis for all of the

claim language.)

None of the cited references teach that lactoferrin works downstream of IL-1β and upstream of TNF-α to inhibit the immune response as set forth in the present specification at page 8, lines 10-12 among other places. Applicants herein add a claim 20 specifically reciting this particular mechanism of action of the presently claimed method in order to even more distinctly claim some embodiments of the present invention.

Applicants respectfully submit that none of the cited references teach or suggest a composition comprising a cosmetic compound that produces a local inflammatory reaction and a lactoferrin product as recited in claim 2. Additionally, none of the cited references teach or suggest a composition comprising a cosmetic compound that produces a local inflammatory response selected from the group consisting of tretinoin, a photoprotective, and a hydroxy acid as recited in claim 3. Notably, these claims are presently withdrawn from consideration.

Applicants further submit that the present invention results from the discovery of particular activities of lactoferrin and/or lactoferrin products that provide tremendous therapeutic advance in treating particular inflammatory diseases. This represents a tremendous advancement over the prior art. It is a well settled principal of the patent law that what might otherwise be unpatentable is rendered patentable by unexpectedly superior results. Hence, for this additional reason, the present claims are patentable.

CONCLUSION

It is believed that the claims are now in condition for allowance and rapid advancement as such is earnestly solicited. If any issues or questions arise that may be resolved by way of a telephonic interview, the Examiner is invited to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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